Remarks

Claims 41-51 are pending in this application upon entry of the claim amendments presented herein. Claim 41 is amended to remove the recitation of "solvate." Claim 52 is canceled in this paper without prejudice to Applicant's right to pursue the subject matter recited by it in one or more divisional, continuation, and/or continuation-in-part applications. No new matter has been introduced.

Applicant respectfully submits that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-10 of the Office Action, claims 41-51 are rejected over Scott *et al.*, *Br. J. Pharmacol.*, 111: 97-102 (1994) ("Scott"), in view of WO 94/00114 by Young *et al.* ("Young") and an excerpt from *Harrison's Principles of Internal Medicine*, 13th Ed., pp. 162-168 (1994) ("Harrison"), and in further view of Gundlah *et al.*, *Pharmacology and Experimental Therapeutics*, 283(2): 581-591 (1997) ("Gundlah"). Applicant respectfully traverses this rejection.

At the outset, Applicant respectfully points out that the Office Action is not fully responsive to the Applicant's response dated October 31, 2007. In particular, after a brief summary of Applicant's arguments presented in the October 31 response, the Office Action concludes, without providing any explanation, that "applicant's ... arguments essentially reiterates (*sic.*) arguments set forth in previous responses to Office actions." (Office Action, page 3). Then, the Office Action simply reproduces the rejections identical to those set forth in previous office actions.[1]

Applicant respectfully points out that the arguments presented in his October 31 response does not "essentially reiterate arguments set forth in previous responses." In particular, as summarized in the Office Action, Applicant submitted that the examiner's allegation that the claims are obvious because "a clear definition is lacking" for the term "enantiomerically pure (S)-didesmethylsibutramine," and thus, racemic didesmethylsibutramine may be encompassed by this term is without merit in view of the fact that the term is clearly defined in the specification so as to exclude the racemic didesmethylsibutramine. (*See* Office Action, page 2). Such a submission had never been made before Applicant's October 31 response, and to the extent that the Examiner's interpretation of the scope of that term affected his assessment of obviousness, it is an important point that should have been considered and addressed by the Examiner.

[1] Applicant notes there is one new rejection at the end of the Office Action.

Despite this, without providing any response or explanation, the Office Action merely dismisses all of the arguments presented in the October 31 response based on the blanket allegation that they "essentially reiterate arguments set forth in previous responses." (*Id.*, page 3). Consequently, Applicant is uncertain as to whether the points provided by Applicant in his responses were properly considered by the Examiner. At the very least, in the case that the Examiner does not find the claims allowable upon reading this paper, Applicant respectfully requests that the next Office Action address the points raised by Applicant clearly and specifically.

Be that as it may, Applicant respectfully submit that the pending claims are not obvious for the following reasons. In the previous Office Action, the Examiner offered the following: 1) "Applicant's conclusory statement that there is no specific suggestion or teaching in the references to combine prior art" is "foreclosed" by the decision in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (Office Action dated October 11, 2007, page 4); 2) Luscombe's teaching that sibutramine and didesmethylsibutramine exhibit similar *in vivo* activities "would reasonably have provided motivation ... to investigate the therapeutic effects of enantiomerically pure (S)-didesmethylsibutramine" (*Id.*, pages 4-5); and 3) "Applicant's assertion that the cited references do not teach enantiomerically pure (S)-didesmethylsibutramine ignores the fact that independent claim 1 encompasses varying degrees of enantiomeric purity," and that "in the absence of a clear specific definition," the term is construed to encompass racemic mixtures. (*Id.*). Applicant respectfully disagrees for at least the following reasons.

First, with regard to the Examiner's allegation that the requirement of specific teaching, suggestion, or motivation ("TSM test") is "foreclosed" by the *KSR* decision, Applicant respectfully points out that the Examiner's position is legally incorrect. Indeed, the *KSR* decision indicated that while the TSM test is not the sole method for determining obviousness, it may still be a factor. (*KSR*, 127 S.Ct. at 1741 ("[w]hen it first established [the TSM test], the Court...captured a helpful insight.")).

Furthermore, Applicant respectfully points out that the Office Action's obviousness contention fails to acknowledge that, in 2007, <u>following</u> the Supreme Court's landmark ruling in *KSR*, the Federal Circuit affirmed the patentability of chiral pharmaceutical compounds. (*See Forest Labs., Inc. v. Ivax Pharmaceuticals, Inc.*, 501 F.3d 1263 (Fed. Cir. 2007), *aff'g* 438 F.Supp.2d 479 (D. Del. 2006)). Similar to the issue in the instant application, *Forest* specifically addressed the issue of whether a single enantiomer of a pharmaceutical compound can be nonobvious and patentable in view of a prior art

disclosure of the pharmaceutical compound's racemate.[2] (*See id.* at 492-96). The Federal Circuit ruled that claims to the single enantiomer pharmaceutical compound were valid and nonobvious. (*See id.*).

In reaching this holding, the Federal Circuit in *Forest* affirmed the "district court's key factual findings underlying its conclusions on obviousness," which are of particular relevance to the obviousness rejection in the instant application. In particular, the District Court determined that the "unpredictable nature of the separation of racemic compounds" meant that "a person skilled in the art seeking such a resolution *would not have a reasonable expectation of success* without undue experimentation." (*See Forest*, 438 F.Supp.2d at 493 (emphasis added); *see also Forest*, 501 F.3d at 1269 ("[T]he district court's key factual findings underlying its conclusions on obviousness are not clearly erroneous.")). In fact, following *KSR*, the Federal Circuit has repeatedly stressed that obviousness determinations in the pharmaceutical arts must involve an assessment of whether a skilled artisan would have possessed a reasonable expectation of success. (*See Forest*, 501 F.3d at 1269; *Takeda Chemical Industries, Ltd. v. Alphapharm Pty. Ltd.*, 492 F.3d 1350, 1360-62 (Fed. Cir. 2007) (finding claimed pharmaceutical compound nonobvious because, inter alia, there existed "no reasonable expectation [of success] in the art.")).

Following Federal Circuit precedent, a U.S. District Court recently upheld the patentability of a single enantiomer drug in view of the prior art disclosure of its racemate. (*See Sanofi-Synthelabo v. Apotex, Inc.*, 492 F.Supp.2d 353, 390 (S.D.N.Y 2007)). Again stressing the importance of determining whether a skilled artisan would have possessed a reasonable expectation of success, the Court concluded that the claimed enantiomer was nonobvious because, *inter alia*, "the prior art did not enable a person of ordinary skill in the art to predict with a reasonable expectation of success whether one enantiomer of [the claimed compound] would have better pharmaceutical properties than the racemate itself . . . .") (emphasis added)).

Additionally, Applicant respectfully invites the Examiner's attention to a decision from the Board of Patent Appeals and Interferences ("BPAI") in *Ex parte Young* (B.P.A.I. Appeal No. 2004-1592), a copy of which is attached hereto as **Exhibit A**, also

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[2] In fact, Applicant respectfully points out that the claims pending in the current application are further removed from the cited prior art references than those at issue in the *Forest* case since the current pending claims recite the use of an optical isomer, rather than the compound itself. Applicant reiterates that no uses claimed by the pending claims were disclosed by any of the references cited by the Examiner, even in connection with racemic didesmethylsibutramine. Therefore, in addition to the obviousness of the compound itself, the obviousness of the recited use should be established for the pending claims to be found obvious.

supports the nonobviousness of the claims under consideration in the instant application.[3] In considering the patentability of claimed methods of treatment using a single enantiomer of a pharmaceutical which was previously disclosed in its racemic form, the BPAI in *Young* held the enantiomer claims to be nonobvious and patentable. The BPAI specifically found "*no reasonable expectation of success* in arriving at appellant's claimed invention" based on the prior art teachings. (*See Young* at 10-11) (emphasis added).

Consequently, taken together, *Forest*, *Sanofi* and *Young* clearly indicate that any allegation that a claimed enantiomer, or its method of use, is obvious in light of its racemate must first establish, on its particularized facts, that a person of ordinary skill would have had a *reasonable expectation of success* in both isolating the claimed enantiomer and using the compound for the purpose recited by the claims. The Office Action made no such determination, and for that reason alone, Applicant respectfully submits that the obviousness rejection should be withdrawn. Further, Applicant respectfully points out that no reasonable expectation of success would have been provided by any of the references cited by the Examiner, alone or in combination, for the following reasons.

In addition, those skilled in the art would have had no basis to "predict with a reasonable expectation of success whether one enantiomer of [the claimed compound] would have <u>better pharmaceutical properties</u> than the racemate itself." (*See Sanofi-Synthelabo*, 492 F.Supp.2d at 390) (emphasis added). As was pointed out previously, the combination of references cited by the Examiner, when read in view of previously submitted Luscombe reference, provide the exact opposite of what is required by this holding to establish a *prima facie* case of obviousness – that *in vivo* activity of didesmethylsibutramine is <u>not</u> significantly better than that of sibutramine.[4] Therefore, Applicant respectfully submits that the references cited by the Examiner fail to establish that there would have been a reasonable expectation that (S)-didesmethylsibutramine would have "better" pharmaceutical properties than racemic didesmethylsibutramine or racemic sibutramine. Applicant respectfully submits that the rejection should be withdrawn for this reason alone.

---

[3] The U.S. patent application under consideration in the unpublished BPAI decision of *Ex parte Young* was application No. 09/238,811, which has common ownership with the instant application. The M.P.E.P. notes that Applicants may cite unpublished BPAI decisions which have common ownership with the application under consideration. *See* M.P.E.P. § 1207.02 ("No unpublished decisions which are unavailable to the general public by reason of 35 U.S.C. 122(a) can be cited by the examiner or the appellant except that either the examiner or the appellant has the right to cite an unpublished decision in an application having common ownership with the application on appeal.").

[4] Moreover, Applicant respectfully submits that the pending claims, which recite, in part, an enantiomerically pure (S)-didesmethylsibutramine, are further removed from Scott and Luscombe.

Moreover, even assuming, *arguendo*, that those skilled in the art were somehow led to investigate (S)-didesmethylsibutramine, its use for the treatment of narcolepsy would still have not been obvious. In this regard, Applicant respectfully points out that the blanket statement that certain symptoms of narcolepsy can be treated with "antidepressants" (as disclosed in Harrison, the third reference cited by the Examiner) does not provide any basis to conclude that any and all antidepressants are effective in treating such symptoms.

This is evidenced by the disclosure of Harrison itself. In the very portion referred to by the Examiner, Harrison, while indicating that antidepressants may be effective in treating certain symptoms of narcolepsy, and that protriptyline is commonly used, also indicates that "compounds including viloxzine hydrochloride and fluoxetine are under evaluation" for narcolepsy. (Harrison, page 167, last paragraph). This clearly implies that each and every antidepressant must be separately evaluated for their efficacy and/or safety for the treatment of narcolepsy, and that purported efficacy of one antidepressant may not be interpolated to any other antidepressants. Thus, Harrison, at most may have rendered the treatment of narcolepsy using (S)-didesmethylsibutramine "obvious to try." As well-settled, "obvious to try" is not a proper legal standard for obviousness, before or after *KSR*. Consequently, Applicant respectfully submits that the combination of references cited by the Examiner would not have led those skilled in the art to arrive at the claimed method.

Finally, with regard to the Examiner's allegation that the term "enantiomerically pure (S)-didesmethylsibutramine" could be interpreted to encompass the racemic mixture, Applicant respectfully points out that such an interpretation is arbitrary and wholly baseless. This is because, contrary to the Examiner's allegation that "a clear specific definition" is lacking for the term in the specification, Applicant respectfully points out that the term is indeed clearly and specifically defined in the specification.

In this regard, Applicant respectfully invites the Examiner's attention to page 5 of the specification. There, it is clearly stated that the term "enantiomerically pure" means one enantiomer of a compound that is "substantially free" of the opposite enantiomer of the compound. (Specification, page 5, lines 16-19). In turn, the specification clearly defines that being "substantially free" of a compound means that the compound is present in less than about 20%, 10%, 5%, or 3% of the weight of the composition. Consequently, based on this clear, specific definition, Applicant respectfully points out that

"enantiomerically pure (S)-didesmethylsibutramine" cannot encompass racemic didesmethylsibutramine, and thus, the Examiner's third allegation is without merit.[5]

B. The Rejection Under 35 U.S.C. § 112 Should Be Withdrawn

On pages 10-12 of the Office Action, claims 41-52 are rejected as allegedly failing to satisfy the written description requirement. In particular, it is alleged that the term "solvate and hydrate" fails to meet the written description requirement. (Office Action, page 11). Although Applicant respectfully disagrees, specifically because the term "solvate and hydrate" is well-known and understood by those skilled in the art, Applicant respectfully points out that the term has been removed from the pending claims solely to expedite the prosecution of this application. In view of this, Applicant respectfully requests that the rejection under 35 U.S.C. § 112 be withdrawn.

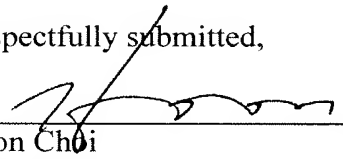
C. Conclusion

For at least the foregoing reasons, Applicant submits that all of the pending claims are allowable, and thus, respectfully requests that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

A fee of $460.00 is believed due for the extension of time. If any additional fees are due for the submission of this paper, the Director is authorized to charge them to Deposit Account No. 50-3013.

Respectfully submitted,

Date May 30, 2008



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[5] Be that as it may, if the Examiner believes that amending claim 1 to specify the term "enantiomerically pure (S)-didesmethylsibutramine" in terms of the weight percentage would expedite the prosecution of this application, Applicant would be amenable to such an amendment.

Exhibit A

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,844	03/17/2000	Timothy J. Barberich	4821-334-999	3697

20582 7590 08/26/2005

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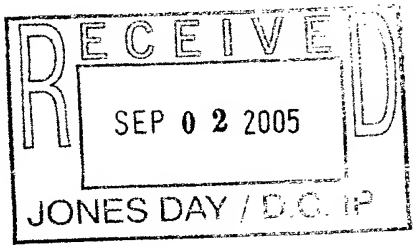
EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.



UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TIMOTHY J. BARBERICH,
PAUL D. RUBIN and WILLIAM E. YELLE

Appeal No. 2005-0906
Application No. 09/527,844

HEARD: July 12, 2005

Before MILLS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-15 and 50-53. Claims 1 and 5 are representative of the subject matter on appeal, and read as follows:

1. A method of treating or prophylaxis of a disorder ameliorated by the inhibition of serotonin reuptake at 5-HT_2 receptors and/or the inhibition of dopamine reuptake at dopamine D_2 receptors in a patient which comprises administering to a patient in need of such treatment or prophylaxis a therapeutically effective amount of a ziprasidone metabolite, or a pharmaceutically acceptable salt, solvate, hydrate, or clathrate thereof.

5. The method of claim 1 wherein the ziprasidone metabolite is ziprasidone sulfoxide or ziprasidone sulfone.

The examiner relies upon the following references:

Lowe, III et al. (Lowe)	4,831,031	May 16, 1989
Allen et al. (Allen)	5,312,925	May 17, 1994

Davis et al. (Davis), "Ziprasidone," CAPlus Abstract, Copyright 2002, American Chemical Society, referencing CNS Drugs, Vol. 8, No. 2, pp. 153-159 (1997).

Prakash et al. (Prakash), "Metabolism and Excretion of a new Antipsychotic Drug, Ziprasidone, in Humans," Drug Metabolism and Disposition, Vol. 25, No. 7, pp. 863-869 (1997).

Claims 1-4 and 6-9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Davis. In addition, claims 1-15 and 50-53 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Davis, Lowe, Allen and Prakash. After careful review of the record and consideration of the issues before us, we reverse both rejections of record.

BACKGROUND

Ziprasidone is a highly potent 5-HT_2 and dopamine D_2 receptor antagonist, and while characterized as an antipsychotic, it may also have anxiolytic and antidepressant effects due to ability to inhibit serotonin and noradrenaline uptake. See Specification, page 1. According to the specification, at least twelve metabolites of ziprasidone have been identified in humans, but ~~that~~ the prior art has reported that the metabolites are not active at the D_2 and 5-HT_{2A} receptor sites. See id. at 1-2.

The specification teaches further that "Ziprasidone offers a number of benefits, but unfortunately many adverse effects are associated with its administration. Examples of adverse affects of ziprasidone include, but are not

limited to, nausea, somnolence, asthenia, dizziness, extra-pyramidal symptoms, akathisia, cardiovascular disturbances, male sexual dysfunction, and elevated serum liver enzyme levels. . . . It is thus desirable to find a compound which possesses advantages of ziprasidone but fewer of its disadvantages." Id. at 2-3.

Thus,

> [t]his invention relates to novel methods using, and compositions comprising, ziprasidone metabolites, preferably, ziprasidone sulfoxide and ziprasidone sulfone. These metabolites, prior to the present invention, have been reported to have little or no in vivo activity. The present invention encompasses the in vivo use of these metabolites, and their incorporation into pharmaceutical compositions and single unit dosage forms useful in the treatment and prevention of disorders that are ameliorated by the inhibition of serotonin reuptake at 5-HT_2 receptors and/or the inhibition of dopamine reuptake at dopamine D_2 receptors. Such disorders include psychotic and neuroleptic disorders. In a preferred embodiment, ziprasidone metabolites are used in the treatment or prevention of neuroleptic and related disorders in mammals, including humans.

Id. at 3.

The specification describes pharmaceutical compositions comprising ziprasidone metabolites, see id. at 7, as well as methods of preparing the sulfoxide and sulfone metabolites, see id. at 7-8.

DISCUSSION

The issues in this case turn primarily on claim construction—specifically the construction of the term "administering" in the claims.

According to the examiner, the term "administering" should be construed as encompassing the administration of the parent drug, ziprasidone, "because metabolites of ziprasidone are necessarily and inevitably formed under normal

condition[s] [sic] once ziprasidone is administered to a patient." Examiner's Answer, page 7.

Appellants argue that the examiner's construction of the term "administering" is contrary to its ordinary meaning. See Appeal Brief, page 10. Appellants argue that "administering" refers to "a compound that exists outside of the patient [which] is given, or applied to the patient." Id. Appellants argue further that the examiner's construction is contrary to unambiguous statements made during prosecution "that the term 'administration' or 'administering,' as used in the claims, means giving to a patient a compound as it exists outside of the body." Id. at 13.

During ex parte prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification as it would be interpreted by the ordinary artisan. See Phillips v. AWH Corp., 2005 WL 1620331, *9 (Fed. Cir.) (en banc) (citing In re Am. Acad. Of Sci. Tech. Ctr., 367 F.3d 1359, 1364 (Fed. Cir. 2004). Thus, it is "entirely appropriate . . . when conducting claim construction to rely heavily on the written description for guidance as to the meaning of the claims." Id.

In the case before us, the specification focuses entirely on the preparation of ziprasidone metabolites, teaching their synthesis and their incorporation into pharmaceutical compositions. Thus, we construe "administering" as used in the claims as requiring the ex vivo preparation of the ziprasidone metabolite, which

is then given to the patient, and excluding giving the patient the parent drug ziprasidone.

Claims 1-4 and 6-9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Davis.[1]

According to the rejection:

> Davis [ ] discloses ziprasidone as an antipsychotic drug having high affinity for serotonin 5-Ht2 and dopamine D2 receptors. Davis [ ] also discloses administration of this drug to patients. Davis further indicates that clinical trials have shown ziprasidone to be effective in treating depression associated with schizophrenia and in reducing anxiety in patients about to undergo dental surgery.

Examiner's Answer, page 3.

It is axiomatic that in order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). As we have construed "administering" as requiring ex vivo preparation of the ziprasidone metabolite, which is then given to the patient, the Davis abstract does not anticipate the claim, as it does not

[1] We note that the examiner relies solely on the abstract of the Davis article, and from our review of the record, it does not appear that the entire reference has been made of record. "Citation of and reliance upon an abstract is generally inappropriate where both the abstract and the underlying document are prior art." MPEP §706.02 (II) (8th edition, Revision 2, May 2004). Moreover, in order for meaningful appellate review to occur, the examiner must present a full and reasoned explanation of the rejection see, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1432 (Fed. Cir. 2002), and that would include analysis of the full underlying document.

teach or suggest the use of metabolites of ziprasidone in that manner. The rejection of claims 1-4 and 6-9 under 35 U.S.C. § 102(b) as being anticipated by Davis is thus reversed.

The examiner asserts that the administration of metabolites of ziprasidone is inherent in the administration of the parent drug, ziprasidone. See Examiner's Answer, page 6. The examiner cites Zenith Laboratories, Inc. v. Bristol Myers Squibb, Co., 19 F.3d 1418, 30 USPQ2d 1285 (Fed. Cir. 1994) in support of that assertion, arguing that case "provides that ziprasidone metabolites are necessarily and inevitably formed from the ziprasidone under normal condition[s] [sic]." Id.

We do not disagree that ziprasidone metabolites are "necessarily and inevitably formed" upon the administration of ziprasidone. Claim 1, however, as construed by the panel, requires the ex vivo preparation of the ziprasidone metabolite, which is then given to the patient. That limitation is neither taught nor suggested by the Davis abstract, and thus the Davis reference does not teach the method of claim 1. The court's decision in Zenith Laboratories is not on point, as the claim at issue in that case was drawn to a compound, and the court construed the claimed compound as not being limited to the compound in its preingested form. See id. 19 F.3d at 1422, 30 USPQ2d at 1288. Thus, the decision in that case, as in the case before us, turned on the construction of the claim, and we have construed the claim to exclude giving the patient the parent drug, ziprasidone.

The examiner argues further that instant claim 1 is analogous to a product-by-process claim, as "the product employed in a method claim[ ] may not be limited to the manipulations of the steps creating the product, only the structure implied by the steps, here, ziprasidone metabolites." Examiner's Answer, page 8. According to the examiner, as the patentability of a product does not depend on its method of production, it is irrelevant to the patentability of the claim whether the ziprasidone metabolite is synthesized ex vivo or produced through the metabolism of the parent drug. See Examiner's Answer, pages 8-9.

We do not find the examiner's reasoning to be persuasive. The claims at issue, such as claim 1, are not product-by-process claims. The claim as construed here requires the ex vivo preparation of the ziprasidone metabolite, which is then given to the patient, and as noted above, the Davis abstract does not teach or suggest giving a ziprasidone metabolite, which has been prepared ex vivo, to a patient.

We note that both the examiner and appellants argue that the holding in Schering Corp. v. Geneva Pharmaceuticals, Inc., 339 F.3d 1373, 67 USPQ2d 1664 (Fed. Cir. 2003) supports their position. In that case, the court held that claims drawn to a loratadine metabolite, DCL, were inherently anticipated by prior art drawn to the administration of loratadine, as "DCL necessarily and inevitably forms from loratadine under normal conditions." Id., 339 F.3d at 1378, 67 USPQ2d at 1668. That holding is distinguishable from the case before us

because the claims are not drawn to the metabolite per se, but to a method of administering the metabolite, which we have construed as requiring ex vivo preparation of the metabolite, which is then given to the patient.

In addition, appellants rely on the following language from Schering. See Appeal Brief, page 11.

> Finally, this court's conclusion on inherent anticipation in this case does not preclude patent protection for metabolites of known drugs. With proper claiming, patent protection is available for metabolites of known drugs. . . .
>
> * * *
>
> A skilled patent drafter, however, might fashion a claim to cover the metabolite in a way that avoids anticipation. For example, the metabolite may be claimed in its pure and isolated form, as in *Kratz* and *Bergstrom*, or as a pharmaceutically composition (e.g., with a pharmaceutically acceptable carrier). The patent drafter could also claim a method of administering the metabolite or the corresponding pharmaceutical composition. The '233 patent would not provide an enabling disclosure to anticipate such claims because, for instance, the '233 patent does not disclose isolation of DCL.

Id., 339 F.3d at 1378, 67 USPQ2d at 1670.

We note that as we need not rely on the above passage from Schering in reaching our decision today, based on our construction of "administering," we decline to address the argument of whether the above passage is dictum, as argued by the examiner, or necessary to the holding in Schering, as argued by appellants.

Claims 1-15 and 50-53 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Davis, Lowe, Allen and Prakash.

Davis is relied upon as above. The examiner states that "Davis does not specifically teach metabolites of ziprasidone, the amounts (i.e., dosage), or routes of administration as instantly claimed." Examiner's Answer, page 4.

Lowe is relied upon for teaching that ziprasidone and ~~their~~ its pharmaceutically acceptable salts may be administered orally, in the form of tablets or capsules, or parentally. Allen is relied upon for teaching the use of ziprasidone hydrochloride as a neuroleptic agent. See id.

Prakash is cited for teaching the affinity of the sulfone and sulfoxide metabolites of ziprasidone for 5HT2 and D2 receptors. See id.

The rejection concludes:

> It would have been obvious to one of ordinary skill in the art at the time of the invention to employ ziprasidone or any of its known salts or metabolites, including the sulfone and sulfoxides, in a method for treating neuroleptic disorders.
>
> One of ordinary skill in the art would have been motivated to employ ziprasidone or any of its known salts or metabolites in a method of treating neuroleptic disorders, because ziprasidone and ziprasidone hydrochloride are known in treating anxiety, depression associated with schizophrenia and situational anxiety (i.e. anxiety prior to dental surgery). Further, employment of different salts and metabolites of a known active, as an alternative form of different salts and metabolites of a known active, as an alternative form of drug delivery, is within the skill of the artisan and therefore obvious.

Id. at 4-5.

"[T]he Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. '[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to

combine the relevant teachings of the references.'" In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citation omitted). An adequate showing of motivation to combine requires "evidence that 'a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.'" Ecolochem, Inc. v. Southern Calif. Edison Co., 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1076 (Fed. Cir. 2000).

As argued by appellants, see Appeal Brief, page 16, Prakash teaches that "[t]he affinities of the sulfoxide and sulfone metabolites for 5-HT_2 and D_2 receptors are low with respect to ziprasidone, and are thus unlikely to contribute to its antipsychotic effects." Prakash, abstract. Thus, the skilled artisan would not have been motivated to substitute the sulfoxide and sulfone metabolites for the ziprasidone parent drug in the methods of Davis, Lowe and Allen. The examiner has therefore not established a prima facie case of obviousness, and the rejection of claims 1-15 and 50-53 under 35 U.S.C. § 103(a) is reversed.

The examiner argues that "Prakash teaches that sulfone or sulfoxide metabolites are major metabolites of ziprasidone . . . and that they possess agonistic affinities towards 5HT2 and D2 receptors. Such agonistic properties would have motivated the skilled artisan to employ sulfone or sulfoxide metabolites in a therapeutic regimen absent information to the contrary." Examiner's Answer, page 11. Moreover, according to the examiner, the fact that "sulfone or sulfoxide metabolites have low affinities towards their receptors is not

persuasive, because such [a] [sic] statement is not an indication that they are void of any value for the same therapeutic purpose as ziprasidone." Id. at 12.

The examiner's argument begs the issue, that is, whether a person of ordinary skill in the art would have been motivated to combine the references to arrive at the claimed invention. Obviousness is determined in view of the sum of all of the relevant teachings in the art, not isolated teachings in the art. See In re Kuderna, 426 F.2d 385, 389, 165 USPQ 575, 578 (CCPA 1970); see also In re Shuman, 361 F.2d 1008, 1012, 150 USPQ 54, 57 (CCPA 1966). In assessing the teachings of the prior art references, the examiner should also consider those disclosures that may teach away from the invention. See In re Geisler, 116 F.3d 1465, 1469, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997). As discussed above, Prakash, although arguably teaching that the sulfone and sulfoxide metabolites have some affinity for the 5-HT_2 and D_2 receptors, specifically teaches that the affinities are low as compared to ziprasidone, and are thus unlikely to contribute to its antipsychotic effects, and thus Prakash would not motivate the ordinary artisan to substitute ziprasidone metabolites for ziprasidone in the method taught by the other references.

CONCLUSION

Based on our construction of "administering" as used in the claims at issue, we reverse the rejection of claims 1-4 and 6-9 under 35 U.S.C. § 102(b) as being anticipated by Davis. Moreover, we also reverse the rejection of claims 1-15 and 50-53 under 35 U.S.C. § 103(a) as being obvious over the combination of Davis, Lowe, Allen and Prakash, as the examiner failed to set forth a prima facie case of obviousness.

REVERSED

Demetra J. Mills
Administrative Patent Judge)
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Eric Grimes) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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